REMARKS

Preliminary Comments

As a preliminary matter, please note the extension of time of three (3) months included with this response and the Request For Continued Examination (RCE).

It is noted that an Information Disclosure Statement (IDS), including a copy of each reference cited therein, was mailed on November 19, 2004. It is requested that the Examiner review the IDS and initial next to each reference listed on the Form PTO-FB-A820 included therewith.

The claims have been amended. Specifically, claims 13, 14 and 45 have been canceled. Claims 2, 15 and 16 have been currently amended. However, no claim fees are due as no new claims have been added.

Claim 2 has been amended to state that the drug is not in the form of a solid dispersion. The amendment has been made to ensure no overlap with Applicants' co-pending US application 10/799,536 or with its parent, issued US patent 6,706,283 B1. Support for the amendment to claim 2 can be found, for example, at page 12 lines 1-8 where it is stated that the drug may be in any form, including in the form of a solid dispersion, indicating that it need not be.

Claim 2 has also been amended (subparagraph (b)) to specify that the drug in the drug-containing composition is a low-solubility drug. Support is in the specification at, for example, the first three lines following the "Background Of The Invention" heading on page 1.

Claims 13 and 14 have been canceled to improve form. These claims were redundant since claim 2 had been previously amended to specify the exact swelling agents. Claims 15 and 16 have accordingly been amended to change their dependency so that they depend from claim 2 rather than from a canceled claim.

Claims 2, 7-9, 12-32, 44, 49-51, 56-57, 63-81, 88-97, 101, 103-108, 118-122, 124, and 130-131 are currently pending in the application.

The Examiner is respectfully requested to reconsider and withdraw the various rejections in light of the comments that follow.

The invention

Applicants' invention solves a particular problem as highlighted in Applicants' previous responses. Applicants' have invented a hydrogel-driven tablet that employs a

highly swelling water-swellable composition that provides efficient release of a drug-containing composition. Such highly swellable materials are desirable for use in conjunction with low solubility drugs suitable for use in the instant invention, such being generally extruded, due to their low solubility, as a viscous suspension. The use of highly swelling materials ensures a more complete extrusion and delivery of the drug.

One of the problems that results from the use of highly swelling water-swellable materials is that such highly swelling materials are generally difficult to compress to a hardness suitable for use. See, for example, page 30, lines 31-33 of the application where it is stated:

> The preferred swelling agents (e.g., those that are highly swelling) are difficult to compress to a hardness suitable for use in the dosage form.

The above problem is by no means trivial from a manufacturing perspective in that, although a highly swelling material for use in the push layer is desirable for its ability to completely or nearly completely extrude the drug composition, such highly swellable materials are generally friable and, as a consequence, it is difficult to make tablets having strength sufficient to reduce the tendency toward chipping and/or breaking during the manufacturing process.

The inventors solved the problem by combining particular swelling agents having a high degree of swelling with a particular tabletting aid to achieve both good release and good tablet strength. As Applicants discuss in greater detail below, the problem is specific to tablets.

The Rejections And Applicants' Traversal

Claim 45 was rejected for indefiniteness. The claim has now been canceled, thus obviating the rejection.

All of the claims, with the exception of claim 57, stand rejected over Wong in view of Stevens, optionally further in view of Park.

The rejection, insofar as it is based on the combination of Wong in view of Stevens appears to be based on substantially the same reasoning as that presented in the previous Office Action (mailed on 10/30/2003), in that the Office Action of 7/26/2004 repeats much of the text in the previous Office Action.

In respect of Stevens, the Examiner stated, among other things, that "...one would be motivated to utilize the instant swelling agent in the expandable hydrogel

portion of Wong's since Stevens et al disclose the advantages of the swelling agent which provides the instant swelling ratio...". Applicants believe the Examiner's reasoning can be roughly summarized as follows: (1) Wong discloses an osmotic device that works like Applicants', but does not teach Applicants' parameters such as the required swelling ratio and core strength, nor the swelling agents or the amount of tabletting aids; (2) Stevens allegedly discloses the swelling agents, including those having a suitable swelling ratio; in example 10 Stevens even discloses a swelling agent containing a combination of sodium starch glycolate (EXPLOTAB) and microcrystalline cellulose (AVICEL). The Examiner appeared to be taking the position that (3) one would be motivated to use the swelling agent of Stevens as the expandable hydrogel in Wong because the Stevens swelling agent provides the required swelling ratio.

In citing Park in conjunction with Wong and Stevens, the Examiner referred to the disclosure in Park of a hydrogel having high mechanical strength and stated that in the controlled drug delivery area superporous hydrogel and superporous hydrogel composites can be used as a platform for long-term oral drug delivery (page 6 of the 7/26/2004 Office Action.

The Examiner rejected claim 57 separately over the references noted above in combination with the Jim Kling article. This rejection is addressed below.

Applicants' Traversal

Applicants' traversal is based in part on the following reasons.

1. Applicants' invention is directed, *inter alia*, to a tablet that combines one of two particular swelling agents with a particular tabletting aid selected from a specifically-identified group, which combination provides a required swelling ratio and a required minimum tablet strength.

2. The combination taught by Applicants are useful in making hard tablets that effect good release of low solubility drugs while at the same time exhibiting high tablet strength so that the tablets do not fracture, and thus fail, during manufacture. One would not, in the absence of Applicants' own specification, look to the combination of references cited by the Examiner because they are not applicable to the problem solved by Applicants. It is Applicants' position that the rejection is based on hindsight.

3. Wong and Stevens are not properly combinable because they are directed to different dosage forms entailing different considerations. The Stevens dosage form in fact teaches away from the instant invention.

Detailed Argument

As a starting point, Applicants note that in order to support an obviousness rejection based on a combination of references, in this case Wong and Stevens (whether or not Park is optionally considered), the prior art must somehow provide a suggestion to make that combination. For example, the Federal Circuit Court has held that it is error for the USPTO to reject a claimed invention as an obvious combination of the teachings of two prior art references when the prior art provided no teaching, suggestion or incentive supporting the combination. "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion, or incentive supporting the combination." *In re Bond*, 910 F2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990); *See also ACS Hospital Systems, Inc. v. Montefiori Hospital*, 732 F.2d 1572, 1577 (Fed. Cir. 1984).

The Federal Circuit Court has further held that, in questions of obviousness, one "cannot pick and choose among the individual elements of assorted prior art references to recreate a claimed invention." *SmithKline Diagnostics, Inc. v. Helena Laboratories Corp.*, 859 F.2d 878, 887, 8 USPQ2d 1468, 1475 (Fed. Cir. 1988).

It is thus Applicants' position that the Examiner has failed to establish a *prima facie* case of obviousness. To establish a *prima facie* case, the Examiner must satisfy three requirements: (1) there must be some suggestion or motivation in the reference or in the knowledge generally available to one of ordinary skill in the art to modify the reference or combine reference teachings; (2) the proposed modification of the prior art must have had a reasonable expectation of success; and (3) the prior art references must teach or suggest all the limitations of the claims. MPEP § 2142.

In support of Applicants' position, Applicants submit that the Examiner has failed to present any teaching or suggestion supporting the combination of Wong and Stevens. Stevens discloses a large number of swelling agents (termed "expandable excipients" therein), as set forth at column 3, lines 26-42, reproduced following:

> In one preferred form, the expandible excipient is a water-swellable hydrogel material. Preferred hydrogel materials are mentioned in WO 90/09168 and include poly(hydroxyethyl-methacrylate), poly(N-vinylpyrrolidone), and polyurethanes. A particularly preferred class of hydrogels are thsoe cross-linked hydrophilic polymers comprising polyethylene oxide residues. Chemical cross-linking may be effected by means of di- or polyisocyanates. Preferably, the polyethylene oxide

> residues have a number average molecular weight greater than 1500, preferably greater than 3,000, and most preferably from 4,000 to 12,000. Particularly preferred polyurethane materials are formed by polymerising a polyethylene glycol with a C_6-C_{10} alkanetriol, and a diisocyanate.

Stevens discloses still more swelling agents, classed as disintegrants, including carboxymethyl starch, sodium starch glycolate, microcrystalline cellulose, carboxymethyl cellulose, and cellulose-2-hydroxypropyl ethers, at column 4, lines 18-31. Stevens makes no suggestion that any one of his swelling agents, out of all those he discloses, is any more preferred than the others. It is respectfully submitted that it would be untenable for one of ordinary skill in the art to zero in on the swelling agent disclosed in Stevens' Example 10 over any other swelling agent (or combination of swelling agents) that Stevens also discloses, but which would clearly be outside the requirements of Applicants' claim 2, and that would not provide the advantages that Applicants specifically sought in respect of manufacturing tablets. The only reason one of ordinary skill would choose the swelling agent of Example 10 is if he or she had the benefit of Applicants' own disclosure. There is simply no suggestion otherwise as between Wong and Stevens to combine the swelling agent of Stevens Example 10, over any of the other Stevens swelling agents, with the tablet of Wong, and no suggestion that any benefit would accrue. And, it is emphatically so well accepted as not to require the citation of supporting law that Applicants' disclosure may not be used as a template to take various components from the prior art and re-assemble them into Applicants' invention. Indeed, that is the essence of a rejection based on the forbidden use of hindsight, as Applicants' respectfully submit has happened here.

It is noted that the Examiner took the position that it would be obvious to use the Stevens swelling agents simply because they are highly swelling. The Examiner appeared to be referring to the highly swelling nature of the Stevens excipients to provide a motivation or incentive to combine the references. Again, however, aside from the fact that no particular swelling ratio is disclosed for Example 10, the Examiner's position applies equally to all of the other swelling agents also disclosed in Stevens, but that are outside Applicants' claims. Thus, according to the Examiner's reasoning it would be equally "obvious", for example, to use microcrystalline cellulose alone as a swelling agent, which would presumably give the required swelling ratio, but which would not give the benefits of good compressibility and hardness required to make a hard tablet having a reduced tendency to fracture during manufacture. Incidentally, in

addition to fact that Stevens does not teach the use of the swelling agent in his Example 10 over, for example, microcrystalline cellulose alone, even if one were to try microcrystalline cellulose alone as a swelling composition, it does not exhibit a swelling ratio of at least 3.5, as required by Applicants' claims.

Even if, for the sake of argument only, one allows that the swelling agent of Stevens Example 10 would be "obvious to try", (1) that particular combination is no more obvious to try than any of the other Stevens swelling agents alone that, in the absence of a tabletting aid, would be outside Applicants' claims. There is no suggestion in Wong or Stevens to use the swelling agent/tabletting aid combination required by Applicants for a tablet, as legally required to sustain an obviousness rejection; and (2) in any case, the law is emphatic that "obvious to try" is NOT the test of obviousness under 35 U.S.C. §103. American Hospital Supply Corp. v. Travenol Laboratories, Inc., 223 USPQ 577, 582 (Fed. Cir. 1984). The Federal Circuit has explained the proper test:

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in light of the prior art. **Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure** (emphasis added).

In re Dow Chemical Co., 5 USPQ2d 1529, 1531 (Fed. Cir. 1988); Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016, 1022-23 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). In the instant case, there is no suggestion to combine Wong and Stevens in the manner required by Applicants' claims. There is not even the barest indication that any advantage would be gained specifically for tablets.

Thus it is respectfully submitted that the combination of Wong and Stevens is not legally or factually tenable. One of ordinary skill in the art would find no suggestion, reason or incentive for selecting the particular swelling agent cited by the Examiner (Stevens Example 10) from among all of the other swelling agents also disclosed in Stevens, which is directed to capsules, and apply it to a tablet as disclosed in Wong. There is simply no reason based on either Stevens or Wong for doing so. Only Applicants have supplied the motivation and incentive for doing so, but to impute that to either reference would be to use that which only Applicants' taught against them. See *W.L. Gore & Associates v. Garlock, Inc.*, 721 F.2d. 1540, 1553, 220 USPQ 303, 308 (Fed. Cir. 1983).

Applicants further emphasize that Stevens is directed to capsules. Even though Stevens discloses that his swelling excipient may take a tablet form (see column 4 lines 1-8 and Example 10), his dosage form itself is a capsule, not a tablet. Applicants submit that the considerations for formulating a capsule are very different from those for formulating a tablet, as Applicants have noted in previous responses. It is known by persons skilled in the art that compared with tablets, powders for filling capsules require the minimum of formulation efforts. See Remington: The Science and Practice of Pharmacy, 19th Ed. (1995) Vol. II at page 1643 (previously submitted). There is no recognition in Stevens that a highly swelling water swellable composition for a tablet must be formulated to combine both a swelling agent with a high degree of swelling and Applicants' tableting aid. Indeed, Stevens et al. states only that his expandible excipient may include "minor amounts of formulating excipients" for the purpose of wetting, improving flow properties, or wicking (Col. 4, lines 32-43), but never mentions or discloses anything relating to achieving hardness in tandem with highly swelling agents. Thus, as a first point, Stevens is clearly unconcerned with excipients that improve tablet hardness. As a second point, Stevens et al. in fact teach away from achieving high hardness in compressed tablets. According to Stevens et al., the hardness of the solid slug used as an excipient in his capsule may be less than that for conventional tablets. Col. 5, lines 3-4. That is the only statement Stevens makes in relation to his excipient "tablets", highlighting that tablet hardness is not an element Stevens is concerned with. One of ordinary skill in the art concerned with making a hard, non-friable tablet would certainly be unenlightened by a publication that specifically disavows the need for tablet hardness.

The examiner continued to cite the Park reference, albeit Park was cited only as an optional secondary reference. The reasons for citing Park appear to be the same as those advanced in previous office actions. The rejection, insofar as it is based on Park, is traversed on the basis that Park fails to remedy the deficiencies of the Wong/Stevens combination. The deficiencies of Wong and Stevens, as discussed above, are incorporated by reference. Park simply relates to a novel swellable hydrogel composition. The material is stated to be formed in part from at least one ethylenically unsaturated monomer such as acrylic or methacrylic acid or a salt or ester thereof, a crosslinking agent, and particles of a disintegrant. Thus Park is clearly concerned with a swelling material different from those now specifically required by Applicants' claims, i.e., sodium starch glycolate and croscarmellose sodium. Just as clearly, there is no

suggestion in Park of the sweller/tabletting aid combination required by Applicants. One of ordinary skill in the art would not find Applicants' invention obvious by substituting Park's hydrogel into Wong's second composition because, *inter alia*, Applicants' claims require a different sweller material that Park discloses nothing about. In different words, Applicants' claims, requiring as they do sodium starch glycolate or croscarmellose sodium as the swelling agent, cannot be obvious over a reference that is focused on a completely different swelling agent.

Claim 57 continues to be rejected over Wong et al. in view of Stevens et al, optionally in further view of Park, and in further view of the Jim Kling article. Applicants traverse the rejection on the basis that it fails to remedy the deficiencies of the Wong/Stevens/optional Park combination, as discussed above. Kling was cited simply for its teaching of Viagra® as a drug for hypertension or erectile function. Wong, Stevens and Park appear to have been cited for the reasons set forth by the Examiner in rejecting the remaining claims. Applicants note that claim 57 depends directly from claim 2. The rejection is traversed on the basis that the combination of Wong and Stevens is fatally defective for the reasons advanced above in Applicants discussion of claim 2 in relation to Wong and Stevens, and Applicants' comments relating to Wong and Stevens are incorporated herein by reference in this respect. It is respectfully submitted that the Kling article, beyond its disclosure of sildenafil citrate, does nothing otherwise to remedy the fatal defects of Wong and Stevens, whether or not those references are combined with Park.

In view of the foregoing comments and amendments, It is accordingly respectfully requested that all rejections be withdrawn. In view of the comments and amendments, this application is believed to be in condition for allowance, and a Notice of Allowance is courteously solicited.

Respectfully submitted,

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James T. Jones
Attorney for Applicant
Reg. No. 30,561

Pfizer Inc
Eastern Point Road
Groton, CT 06340
(860) 441-4903